

WHAT IS CLAIMED IS:

1. An isolated polypeptide comprising at least 10 contiguous amino acids of SEQ ID NO: 2, 4, 5 or 6.

5 2. The polypeptide of claim 1, comprising at least 15 contiguous amino acids of SEQ ID NO: 2, 4, 5 or 6.

3. The polypeptide of claim 2, comprising at least 20 contiguous amino acids of SEQ ID NO: 2, 4, 5 or 6.

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4. The polypeptide of claim 3, comprising at least 25 contiguous amino acids of SEQ ID NO: 2, 4, 5 or 6.

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5. The polypeptide of claim 4, comprising at least 30 contiguous amino acids of SEQ ID NO: 2, 4, 5 or 6.

6. The polypeptide of claim 5, comprising at least 50 contiguous amino acids of SEQ ID NO: 2 or 4.

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7. The polypeptide of claim 6, comprising an amino acids sequence of SEQ ID NO: 2, 4, 5 or 6..

8. The polypeptide of claim 1, further comprising a leader sequence operatively coupled to the amino terminus of the polypeptide.

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9. The polypeptide of claim 8, wherein the leader signal sequence is a Kaposi fibroblast growth factor signal sequence, HIV-1 Tat (48-60), D-amino acid-substituted HIV-1 Tat (48-60), arginine-substituted HIV-1 Tat (48-60), Drosophila Antennapaedia (43-58), or a polyarginine polypeptide having at least 6 to 8 arginines.

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10. An isolated polynucleotide comprising a nucleic acid encoding a RAIN polypeptide.

5 11. The polynucleotide of claim 10, wherein the nucleic acid sequence is as set forth in SEQ ID NO:1 or SEQ ID NO:2.

12. A method of treating a subject with bone loss comprising inhibiting osteoclast precursor cell fusion by administering a RAIN polypeptide in amount effective to modulate RANK signaling.

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13. A method of treating a subject with bone loss comprising inhibiting osteoclast precursor cell fusion by administering an effective amount of an expression vector, wherein the expression vector comprises a polynucleotide encoding a RAIN polypeptide under the transcriptional control of a promoter.

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14. The method of claim 13, wherein the promoter is a constitutive promoter.

15. The method of claim 13, wherein the promoter is an inducible promoter.

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16. The method of claim 13, wherein the expression vector comprises a viral vector.

17. The method of claim 13, wherein said administration is repeated.

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18. The method of claim 16, wherein the viral vector is selected from the group consisting of vaccinia virus, adenovirus, herpesvirus, retrovirus, cytomegalovirus, and adeno-associated virus.

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19. The method of claim 13, wherein said expression vector is delivered endoscopically, intraveneously, intraarterially, intramuscularly, intralesionally, percutaneously, or subcutaneously.

20. A method for inhibiting osteoclast precursor cell fusion comprising contacting an osteoclast precursor cell with an expression vector that expresses a RAIN polypeptide.
- 5 21. The method of claim 20, wherein the expression vector is a plasmid expression vector.
22. The method of claim 21, wherein the expression vector is a viral expression vector.
- 10 23. A method of identifying a modulator of a osteoclast precursor fusion comprising:
 (i) providing a cell deficient in a RAIN polypeptide;
 (ii) contacting the cell with a candidate substance; and
 (iii) comparing osteoclast cell fusion observed when the candidate substance is not added, wherein an alteration in osteoclast cell fusion indicates that the candidate substance is a modulator of a osteoclast cell fusion.
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24. The method of claim 23, wherein the candidate substance is a second cell, a cancer cell, a multiple myeloma cell, a peptide, a peptide mimetic or a small molecule.
- 20 25. The method of claim 23, wherein the candidate substance is selected from a small molecule library.
26. The method of claim 23, wherein the candidate substance is a protein.
- 25 27. The method of claim 23, wherein the candidate substance is a RAIN analogue.
28. The method of claim 23, wherein the cell deficient in a RAIN polypeptide comprises an inactivated RAIN gene.
- 30 29. The method of claim 23, wherein the cell deficient in a RAIN polypeptide expresses an antisense RAIN nucleic acid.